

# ABC of the upper gastrointestinal tract

## Indigestion: When is it functional?

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Patients often complain of indigestion, but what do they mean? Indigestion is an old English word that means lack of adequate digestion, but patients and doctors interpret this in different ways. Many patients mean heartburn or acid regurgitation, the classic symptoms of gastro-oesophageal reflux disease. Some describe belching, abdominal rumblings, or even bad breath as indigestion. Others mean pain localised to the epigastrium or a non-painful discomfort in the upper abdomen which may be described as fullness, bloating, or an inability to finish a normal meal (early satiety). Dyspepsia is best restricted to mean pain or discomfort centred in the upper abdomen.

There are many causes of dyspepsia, but at least two thirds of patients have no structural or biochemical explanation for their symptoms. It has been suggested that dyspepsia can be subdivided based on groups (or clusters) of symptoms. However, subgroups have not proved to be of value in identifying the underlying cause of dyspepsia and overlap considerably. Some patients report having troublesome burping associated with abdominal bloating or discomfort that is transiently relieved by bringing up the wind. These patients have aerophagy, and repeated swallowing of air may be obvious during the consultation.

## Causes of dyspepsia

History taking is key to identifying the likely cause of dyspepsia.

### Gastro-oesophageal reflux disease

It is important and practical to distinguish gastro-oesophageal reflux disease (GORD) from dyspepsia. Frequent heartburn is a cardinal symptom of GORD; acid reflux causes a retrosternal or epigastric burning feeling that characteristically radiates up towards the throat, is relieved transiently by antacids, and is precipitated by a meal or by lying down.

Up to 60% of people with upper gastrointestinal symptoms report both heartburn and epigastric pain or discomfort. This overlap can be confusing, but it is not the presence of a symptom but its predominance that is most helpful clinically. For example, if the main complaint is a burning epigastric pain that radiates up towards the throat then this is highly predictive of GORD (as can be objectively demonstrated by abnormal results from 24 hour oesophageal pH monitoring).

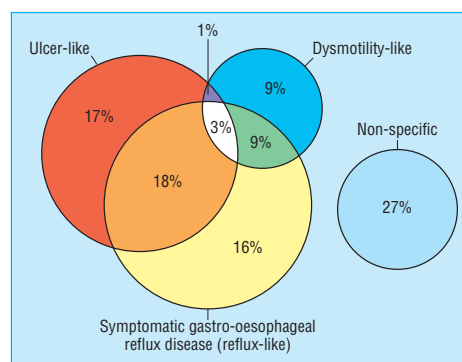
Reflux oesophagitis can be detected at endoscopy, but over half of patients with true GORD will not have evidence of mucosal breaks (erosions). Oesophageal erythema or the presence of a hiatal hernia are unreliable signs that cannot be used to determine if a patient has reflux disease. Although some patients are unable to adequately describe their symptoms or decide which is their predominant complaint, if a detailed history is taken a clinical diagnosis of GORD can be made in most cases, including those in whom endoscopy is normal.

### Peptic ulcers

Many textbooks continue to propagate the myth that symptoms can accurately identify peptic ulcer disease. Unfortunately, classic ulcer symptoms (such as postprandial epigastric pain or night pain) often occur in patients with functional dyspepsia, and many patients with an ulcer have atypical complaints.

### Major structural causes of dyspepsia

- Chronic peptic ulcer (duodenal or gastric)
- Gastro-oesophageal reflux disease (> 50% have no oesophagitis)
- Gastric or oesophageal adenocarcinoma (rare but of concern for patient and doctor)



Overlap of subgroups of dyspepsia based on symptoms in patients with documented functional dyspepsia

### Uncommon causes of upper abdominal pain or discomfort that may be confused with dyspepsia

- Aerophagy (repetitive belching from air swallowing)
- Biliary colic from gall stones
- Abdominal wall pain (a clinical clue is localised tenderness on palpation not reduced by tensing the abdominal wall muscles)
- Chronic pancreatitis (episodic dull steady upper abdominal pain that may be aggravated by meals and radiate through to the back)
- Malignancy (such as of pancreas or colon)
- Mesenteric vascular insufficiency (postprandial pain, weight loss, and a fear of eating)
- Angina
- Metabolic disease (such as diabetes, renal failure, hypercalcaemia)

### Conditions to be recognised from a patient's history

#### Symptomatic gastro-oesophageal reflux disease

- Burning retrosternal or epigastric pain or discomfort radiating upwards towards the throat and relieved, albeit transiently, by antacids
- Regurgitation of acid

#### Irritable bowel syndrome

- Abdominal pain plus an erratic disturbance of defecation linked to the pain (such as pain relief with defecation, looser or harder stools with pain onset, or more frequent or less frequent stools with pain onset)

#### Biliary tract disease

- Biliary-type pain

#### Peptic ulcer

- Classic ulcer symptoms do not distinguish peptic ulcer disease from functional dyspepsia

Endoscopy remains the test of choice to rule out chronic peptic ulceration, but its presence can now be inferred by indirect testing. *Helicobacter pylori* causes 90% of duodenal ulcers and 70% of gastric ulcers; aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) account for most of the remainder. Patients who are not infected with *H pylori* and not taking NSAIDs have a very low probability of ulcer disease.

### Gastric cancer

Fear of gastric cancer is one of the main reasons why patients with dyspepsia present to their general practitioner. Gastric cancer is found in less than 2% of all cases referred for endoscopy. Early gastric cancer comprises only 10% of cancer cases, but it is important to diagnose because it is curable and 60-90% of patients initially present with dyspepsia.

However, the risk of gastric cancer is extremely low in patients under the age of 55 years presenting with the new onset of dyspepsia in most Western countries including Britain. Furthermore, "alarm" symptoms such as weight loss, dysphagia, or anaemia help to identify those who need to be investigated in order to exclude malignancy, although between 15% and 50% of dyspeptic patients with gastric cancer do not have these symptoms. Endoscopic evaluation is therefore recommended in older patients presenting with new symptoms and in all patients with alarm symptoms.

### Gall stones

Ultrasonography will detect gall stones in a minority of patients with apparently unexplained dyspepsia. However, gall stones are common and often incidental in the absence of biliary symptoms. Biliary colic is characteristically severe, episodic, and constant (rather than colicky) pain in the epigastrium or right upper quadrant typically lasting one to several hours. This can usually be easily distinguished from the pain or discomfort of functional dyspepsia.

While many patients with gall stones also complain of bloating, nausea, and other vague upper abdominal symptoms, these complaints are just as common in patients without gall stones. Moreover, cholecystectomy does not reliably result in long term relief of any of these vague complaints and cannot be recommended. Cholecystectomy in a patient with non-biliary type pain is likely to result in the patient at a later date being labelled as having the post-cholecystectomy syndrome.

### Functional dyspepsia

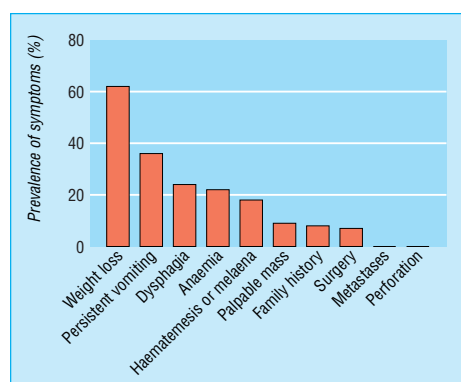
Most commonly, either no abnormalities or irrelevant abnormalities (such as gastric erythema or a few gastric erosions) are found at endoscopy; these patients are labelled as having functional (or non-ulcer) dyspepsia. As antisecretory drugs may result in healing of ulcers or oesophagitis (and hence lead to a misdiagnosis of functional dyspepsia), these drugs are best not started before endoscopy if possible.

## Functional dyspepsia

### Pathogenesis

The pathogenesis of functional dyspepsia remains uncertain. *H pylori* gastritis is detected in about half of patients with functional dyspepsia, but it is also common in otherwise asymptomatic people. The question of whether this infection causes symptoms in patients without ulcer disease has been controversial. There is no evidence that specific symptoms identify those with *H pylori* infection. Acid secretion is usually normal in patients with functional dyspepsia, except perhaps in a subset infected with *H pylori*.

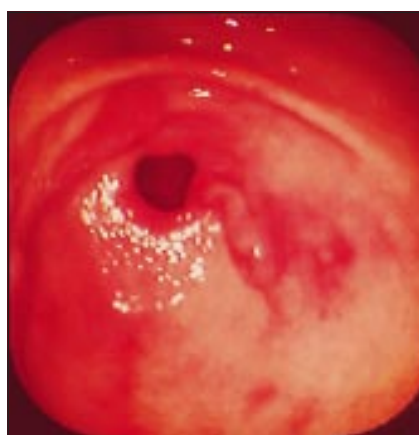
In functional dyspepsia gastric (and duodenal) sensation is disturbed (the "irritable stomach"), and in about half of patients



Prevalence of "alarm" symptoms in patients with gastric cancer

### Alarm symptoms

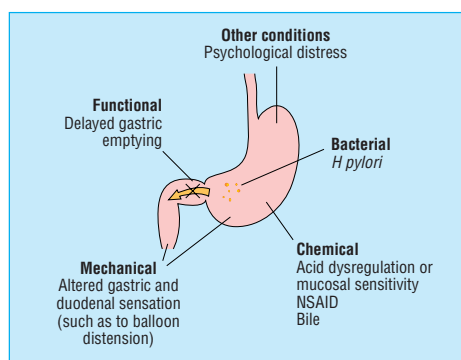
- Anorexia
- Loss of weight
- Anaemia due to iron deficiency
- Recent onset of persistent symptoms
- Melaena, haematemesis
- Dysphagia



Antral erythema and erosions in patient with functional dyspepsia

### Practice point

**If possible, H<sub>2</sub> receptor antagonists and proton pump inhibitors should not be started before endoscopy (or should be stopped at least two weeks before endoscopy)**



Pathogenesis of functional dyspepsia

distension induces symptoms at lower pressures or volumes than it does in healthy people. Delayed gastric emptying can be detected in a quarter to a half of patients with functional dyspepsia. In addition, a subset of patients have altered intragastric distribution of food, which reflects abnormal proximal gastric relaxation (a “stiff” fundus). There is an increased probability of detecting gastric motor abnormalities in women and possibly in those with severe postprandial fullness or severe vomiting.

There is controversy as to whether functional dyspepsia is a “forme fruste” of the irritable bowel syndrome, and both conditions may overlap. About a third of patients with functional dyspepsia have an erratic disturbance of defecation closely linked to their pain, and probably truly have irritable bowel syndrome. There is also evidence of gut hypersensitivity in both functional dyspepsia and the irritable bowel syndrome.

Smoking and alcohol do not seem to be important in functional dyspepsia, but coffee ingestion has been linked to exacerbation of symptoms. Some patients with functional dyspepsia suffer from an anxiety disorder or depression, but whether this is cause or effect remains unclear.

### Identification and management

#### Investigation versus testing for *H pylori*

The devil is in the detail, and a careful detailed appraisal of a patient's history with a judicious approach to testing is necessary. Older patients or those with alarm features warrant prompt referral for endoscopy and further investigations as required. Testing for *H pylori* infection will help in guiding management in the remainder; between 20% and 60% of those with *H pylori* infection will have peptic ulcer disease.

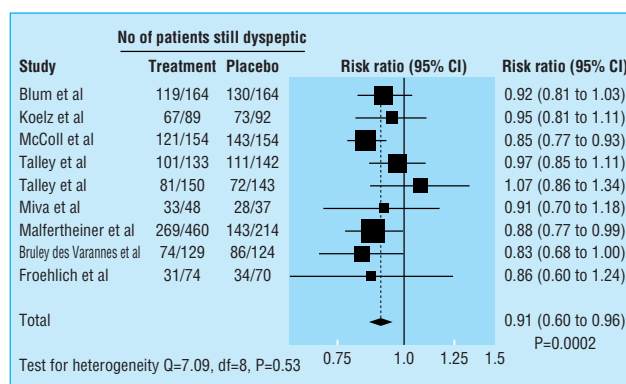
For patients with *H pylori* infection, one course of action is to refer them for endoscopy to determine who has peptic ulcer disease or functional dyspepsia (the two main considerations) and plan treatment accordingly (the “test and endoscope” strategy). Alternatively, a reasonable course of action is to treat infected patients with appropriate antibiotics and observe the clinical course (the “test and treat” strategy). Although treatment of infection may not cure functional dyspepsia (see below), it will usually eliminate the peptic ulcer diathesis and hence will often relieve the symptoms. Moreover, recent trials suggest that “test and treat” is a safe and cost effective strategy that results in a long term outcome similar to that with a strategy of prompt endoscopy. Hence, “test and treat” has been gaining widespread acceptance.

#### Principles of management

Reassurance and explanation remain the key elements in managing documented or suspected functional dyspepsia. Patients should be advised that this is a real condition and that their symptoms are not imaginary. Furthermore, they should be advised that the condition never leads to cancer or other serious disease. Patients' fears should be identified and addressed. Modification of diet (such as avoiding foods that provoke symptoms and adopting a low fat diet because high fat foods may impair gastric emptying) and stopping medications can be helpful. Antacids are no better than placebo in functional dyspepsia, but notably the placebo response ranges between 20% and 60%.

#### Initial treatment

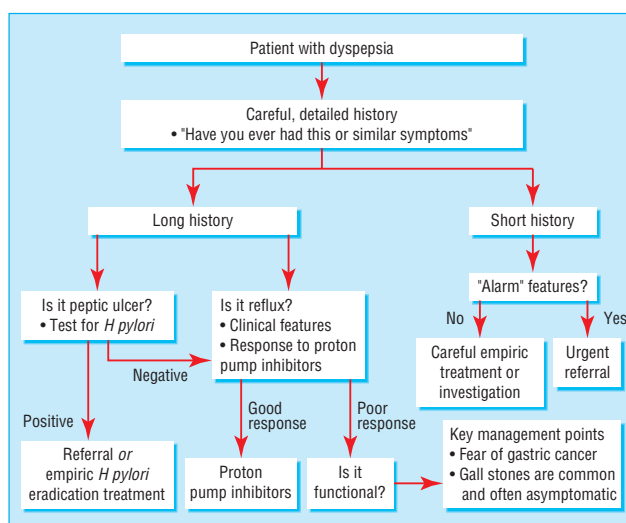
In patients with a diagnosis of functional dyspepsia, a short term therapeutic trial for four weeks with an acid suppressant is worth while. Symptom subgroups may be of some help in predicting a patient's response to treatment if a predominant



Results of systematic review comparing *H pylori* eradication treatment for non-ulcer dyspepsia with placebo

### Initial management of functional dyspepsia

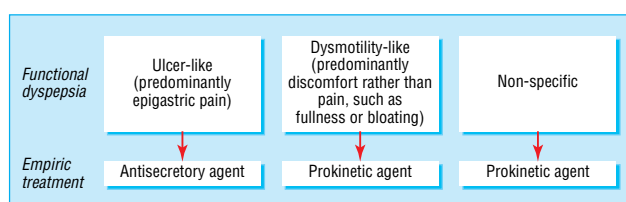
- Make a positive clinical diagnosis
- Minimise investigations and don't repeat tests without good reason
- Determine the patient's agenda and identify psychosocial stressors
- Find out why the patient has presented now
- Provide education and reassurance



Algorithm for management of functional dyspepsia

### Drugs that are most likely to cause dyspepsia

- Non-steroidal anti-inflammatory drugs
- Digoxin
- Antibiotics (macrolides, metronidazole)
- Corticosteroids, oestrogens
- Iron, potassium chloride
- Levodopa
- Theophylline
- Quinidine
- Niacin, gemfibrozil
- Colchicine



Empiric treatment for functional dyspepsia

symptom can be identified, but relying on clusters of symptoms is generally not useful.

H<sub>2</sub> receptor blockers are, at best, of only modest efficacy in functional dyspepsia. While some trials suggest that they are superior to placebo, other trials have not shown any additional benefit. Proton pump inhibitors are more efficacious than placebo in functional dyspepsia (by about 10-20%), but not in the subgroup of patients with dysmotility-like dyspepsia.

If a patient fails to respond to an antisecretory drug after four weeks, it is reasonable to consider increasing the dose or switching to an alternative or a prokinetic drug. If the patient has failed to respond after eight weeks, then it is reasonable to refer the case to a specialist for further evaluation.

Eradicating *H pylori* infection cures functional dyspepsia in only a minority of cases. A meta-analysis has suggested a small therapeutic gain over 12 months follow up (15 needed to be treated to cure one case). Whether sucralfate or bismuth is better than placebo in treating functional dyspepsia is unclear, but it is unlikely; misoprostol may actually aggravate symptoms and cause diarrhoea in some patients.

#### Long term management

Functional dyspepsia is generally a relapsing and remitting condition. Treatment should not be prolonged, and frequent drug holidays should be prescribed. In patients with symptoms that are difficult to control a trial of an antispasmodic or antidepressant may be useful, but specialist referral to confirm the diagnosis and exclude rare causes of dyspepsia should first be considered. Some patients will benefit from behavioural therapy or psychotherapy.

#### Aerophagy

Air swallowing is often extremely resistant to treatment. Options include avoidance of chewing gum, aerated drinks, and smoking; use of anti-gas agents (such as activated dimeticone or charcoal); and relaxation therapy. However, no treatment is of proved benefit, and anti-gas agents are no better than placebo.

The graph of prevalence of alarm symptoms in patients with gastric cancer is adapted from Gillen D, McColl KE. *Am J Gastroenterol* 1999;94:75-9. The forest plot comparing *H pylori* eradication treatment with placebo is reproduced from Moayyedi P, et al. *BMJ* 2000;321:659-64.

*BMJ* 2001;323:1294-7

#### Treatment for functional dyspepsia

##### Initial treatment

- Antisecretory drug (H<sub>2</sub> receptor blocker, proton pump inhibitor) or
- Prokinetic drug (domperidone) if antisecretory treatment fails
- Switch treatment if first drug type fails

##### Resistant cases (failed initial treatment)

- *H pylori* eradication
- Sucralfate or bismuth
- Antispasmodic agent (such as mebeverine)
- Antidepressant (such as selective serotonin reuptake inhibitor or tricyclic drug)
- Behavioural therapy or psychotherapy
- No treatment is proved to be of benefit in these patients

#### When to consider referring a dyspeptic patient to a specialist

- If prompt investigation is required (such as recent onset of alarm symptoms)
- Severe pain
- Failure of symptoms to resolve or substantially improve after appropriate treatment
- Progressive symptoms

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#### A memorable patient

##### To cure a mockingbird

Many years ago, I daily visited a gentle family man who was terminally ill in bed. He was 80 years old and a widower, and was supported by his daughter, who lived with him.

One day I found him lying propped up on his bed and looking in a distressed state at the cuckoo clock hanging on the opposite wall. When I asked how he was feeling he told me: "I am very miserable as the cuckoo has died." He certainly looked very upset, and he told me that the clock had been bought for himself and his wife when they were married and he could not bear to think that it had "died."

To comfort him, I took a chair and climbed up to see this other invalid. Being an organist, I was fascinated to discover that the sounds of the cuckoo were produced by two organ pipes. There were two small bellows attached to wire levers, which were powered by a rotating wheel on the hour similar to the bell in a chiming clock. I gently lifted out the pipes: one was voiced with a low set upper lip as a diapason, and the other with a high curved upper lip as a flute. Hence, one made the sound "Cuck," and the other said "Ooh."

The mechanism was old and dry, so I cleaned it and greased it with fat and then turned the pointer. Out came the bird, and the mechanism was working again. I said, "Right, I think he is healed—just watch." The patient watched as I inserted the pipes and then turned the hands. Out came the bird but, to my dismay, cried, "Ooh-cuck, Ooh-cuck."

I had obviously replaced the pipes in the wrong order, and the old man looked even more devastated than ever and said, "Oh, what have you done to my poor bird?" As I quickly reassured him that all would be well, I removed the pipes again and set them in their correct order. I then turned the hands to 12 o'clock and with him listened as the bird came out singing "Cuckoo" twelve times.

His countenance was transformed, and he looked at me with profound gratitude and said, "Oh what a wonderful doctor you are." It turned out to be a happy visit despite the circumstances.

John Richardson *general practitioner, Belle-vue, Ryton, Tyne and Wear*